Robbins PATHOLOGIC BASIS OF DISEASE

5th Edition

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W.B. SAUNDERS COMPANY
A Division of Harcourt Brace & Company
Philadelphia London Toronto Montreal Sydney Tokyo

W.B. SAUNDERS COMPANY
A Division of
Harcourt Brace & Company

The Curtis Center
Independence Square West
Philadelphia, Pennsylvania 19106

Library of Congress Cataloging-in-Publication Data

Cotran, Ramzi S.
Robbins pathologic basis of disease. —5th ed. / Ramzi S. Cotran, Stanley L. Robbins, Vinay Kumar.
p. cm.
Includes bibliographical references and index.
ISBN 0-7216-5032-5
1. Pathology. I. Robbins, Stanley L. (Stanley Leonard).
II. Kumar, Vinay. III. Title. IV. Title: Pathologic basis of disease.
[DNLM: 1. Pathology. QZ 4 C845r 1994]
RB111.R62 1994
616.07—dc20
DNLM/DLC 94-2629

Robbins Pathologic Basis of Disease, 5th edition ISBN 0-7216-5032-5

Printed in the United States of America.

Last digit is the print number: 9 8 7 6 5 4

are of the supressor-cytotoxic phenotype, expressing CD8 molecules on their surfaces.

ERYTHEMA NODOSUM AND ERYTHEMA INDURATUM

Panniculitis is an inflammatory reaction in the subcutaneous fat that may affect (1) principally the connective tissue septa separating lobules of fat, or (2) predominantly the lobules of fat themselves. *Erythema nodosum* is the most common form of panniculitis and usually has an acute presentation. Its occurrence is often associated with infections (beta-hemolytic streptococcal infection, tuberculosis, and, less commonly, coccidioidomycosis, histoplasmosis, and leprosy), drug administration (sulfonamides, oral contraceptives), sarcoidosis, inflammatory bowel disease, and certain malignancies, but many times a cause cannot be elicited. Many types of panniculitis have a subacute to chronic course.

Panniculitis often involves the lower legs. Erythema nodosum presents acutely as poorly defined, exquisitely tender, erythematous nodules that may be better felt than seen. Fever and malaise may accompany the cutaneous signs. Over the course of weeks, lesions usually flatten and become bruise-like, leaving no residual clinical scars, while new lesions develop. Biopsy of a deep wedge of tissue is usually required to establish a definitive diagnosis.

Erythema induratum is an uncommon type of panniculitis that affects primarily adolescents and menopausal women. Although the cause is not known, most observers today regard this disorder as the result of a primary vasculitis affecting deep vessels supplying lobules of the subcutis, with subsequent necrosis and inflammation within the fat. Erythema induratum presents as an erythematous, slightly tender nodule that usually goes on to ulcerate. Originally considered a hypersensitivity response to tuberculosis, erythema induratum today most commonly occurs without an associated underlying disease.

MORPHOLOGY. The histopathology of erythema nodosum is distinctive. In early lesions, there is widening of the connective tissue **septa** owing to edema, fibrin exudation, and neutrophilic infiltration (Fig. 26–20). Later, infiltration by lymphocytes, histiocytes, multinucleated giant cells, and occasional eosinophils is associated with septal fibrosis. Vasculitis is not present. In erythema induratum, on the other hand, the fat **lobule** is involved by granulomatous inflammation and zones of caseous necrosis. Early lesions show necrotizing vasculitis affecting small to medium-sized arteries and veins in the deep dermis and subcutis.

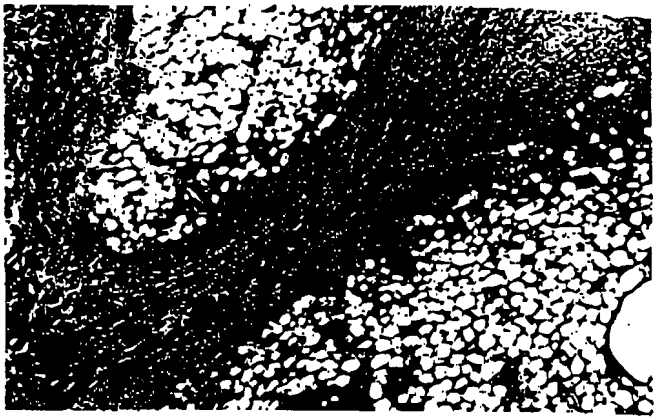

Figure 26–20. Erythema nodosum. A septum of the subcutaneous fat is preferentially infiltrated and widened by inflammatory cells.

Erythema nodosum and erythema induratum are but two examples of many types of panniculitis. *Weber-Christian disease (relapsing febrile nodular panniculitis)* is a rare form of lobular, nonvasculitic panniculitis seen in children and adults. It is marked by crops of erythematous plaques or nodules, predominantly on the lower extremities, created by deep-seated foci of inflammation with aggregates of foamy histiocytes admixed with lymphocytes, neutrophils, and giant cells. *Factitial panniculitis*, as a result of self-inflicted trauma or injection of foreign or toxic substances, is a form of secondary panniculitis that often poses profound problems in definitive clinical and pathologic diagnosis and may present a distinct set of therapeutic challenges. Deep mycotic infections in immunocompromised individuals may produce histologic changes that mimic primary panniculitis. Finally, disorders such as lupus erythematosus (see later) may occasionally have deep inflammatory components with associated panniculitis.

CHRONIC INFLAMMATORY DERMATOSES

This category focuses on those persistent inflammatory dermatoses that exhibit their most characteristic clinical and histologic features over many months to years. Unlike the normal cutaneous surface, the skin surface in some chronic inflammatory dermatoses is roughened as a result of excessive or abnormal scale formation and shedding (desquamation) (Fig. 26–21). However, not all scaling lesions are inflammatory. Witness the hereditary ichthyoses with fish-like scales as the result of some de-

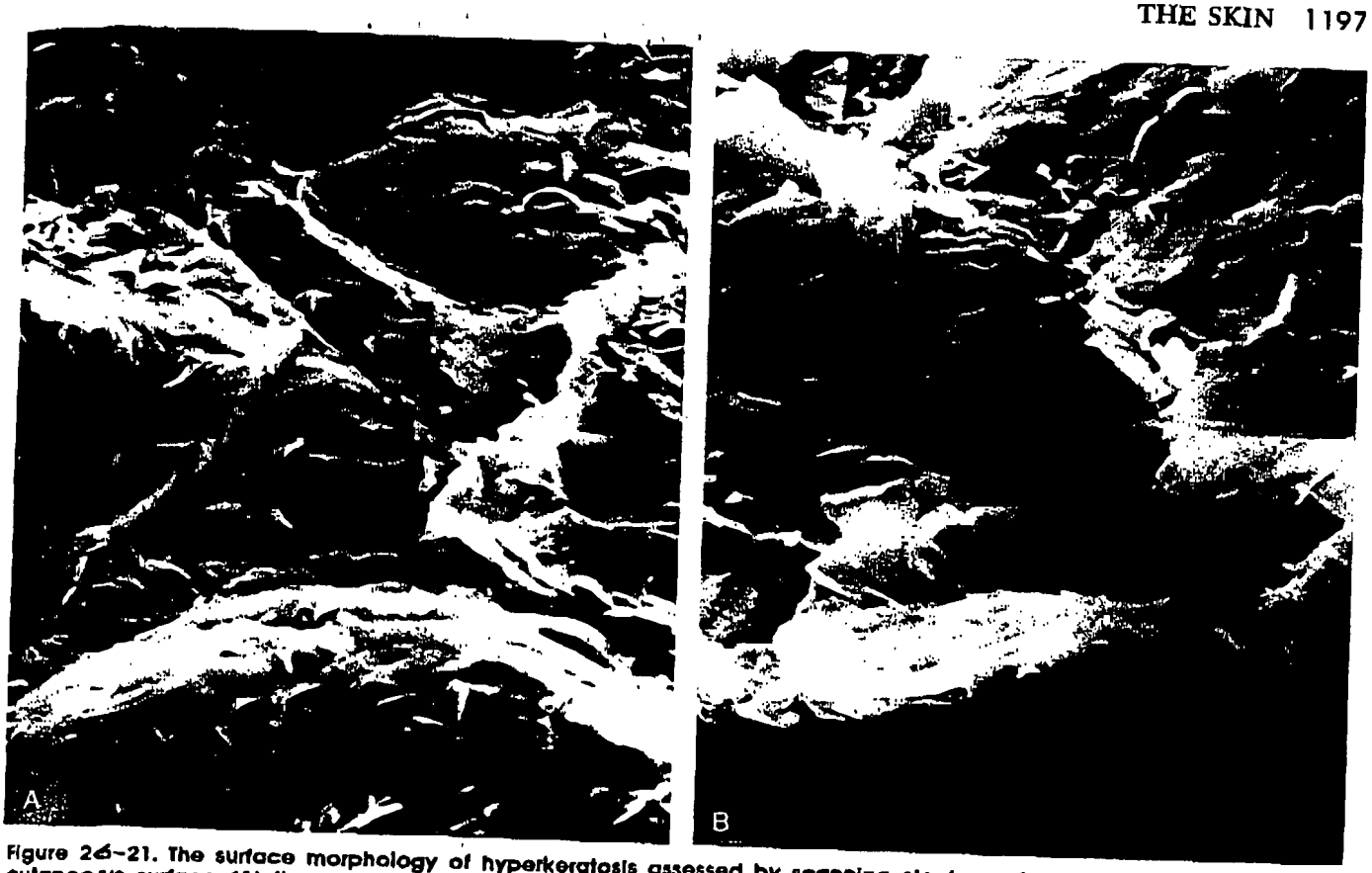

Figure 26-21. The surface morphology of hyperkeratosis assessed by scanning electron microscopy. Unlike the normal cutaneous surface *(A)* that is covered by relatively smooth and contiguous squamous cells of the stratum corneum, chronic dermatoses often exhibit excessive stratum corneum production *(B)*, producing an irregular and roughened surface. (Courtesy of Dr. Robert Lavker, University of Pennsylvania.)

fect in the adhesive properties of cells in the stratum corneum.

PSORIASIS

Psoriasis is a common chronic inflammatory dermatosis affecting as many as 1 to 2% of people in the United States. Persons of all ages may develop the disease. Psoriasis is sometimes associated with arthritis, myopathy, enteropathy, spondylitic heart disease, and AIDS. Psoriatic arthritis may be mild or produce severe deformities resembling the joint changes seen in rheumatoid arthritis.

Clinically, psoriasis most frequently affects the skin of the elbows, knees, scalp, lumbosacral areas, intergluteal cleft, and glans penis. The most typical lesion is a well-demarcated, pink to salmon-colored plaque covered by loosely adherent scales that are characteristically silver-white in color (Fig. 26–22). Variations exist, with some lesions occurring in annular, linear, gyrate, or serpiginous configurations. Psoriasis can be one cause of total-body erythema and scaling known as *erythroderma*. Nail changes[53] occur in 30% of cases of psoriasis and consist of yellow-brown discoloration (often likened to an oil slick), with pitting, dimpling, separation of the nail plate from the underlying bed (onycholysis), thickening, and crumbling. In the rare variant called *pustular psoriasis*, multiple small pustules form on erythematous plaques. This type of psoriasis is either benign and localized (hands and feet) or generalized and life-threatening, with associated fever, leukocytosis, arthralgias, diffuse cutaneous and mucosal pustules, secondary infection, and electrolyte disturbances.

MORPHOLOGY. Established lesions of psoriasis have a characteristic histologic picture. Increased epidermal cell turnover results in marked epidermal thickening (acanthosis), with regular downward elongation of the rete ridges. Mitotic figures are easily identified well above the basal cell layer, where, in normal skin, mitotic activity is confined (Fig. 26–23). **The stratum granulosum is thinned or absent, and extensive overlying parakeratotic scale is seen.** Typical of psoriatic plaques is thinning of the portion of the epidermal cell layer that overlies the tips of dermal papillae (suprapapillary plates) and dilated, tortuous blood vessels within

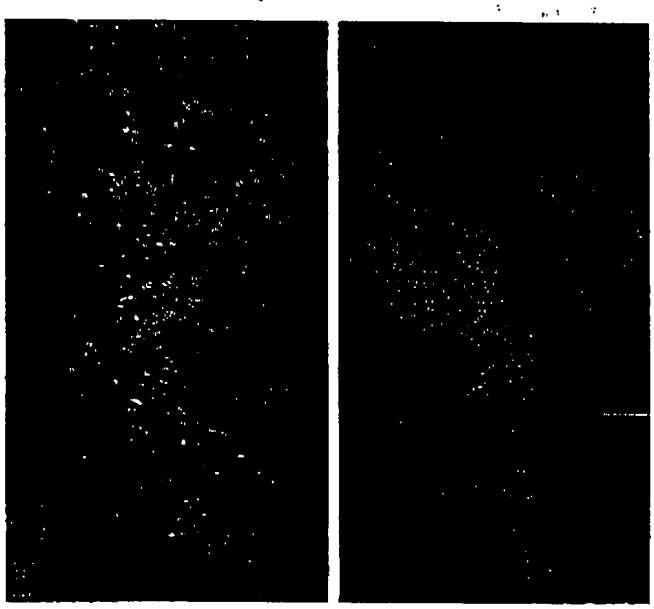

Figure 26–22. Clinical evolution of psoriasis. Early and eruptive lesions may be dominated by signs of inflammation and erythema *(left panel)*. Established, chronic lesions demonstrate erythema surmounted by characteristic silver-white scale *(right panel)*. Rarely, the early inflammatory phase predominates throughout the course of the disease (pustular psoriasis).

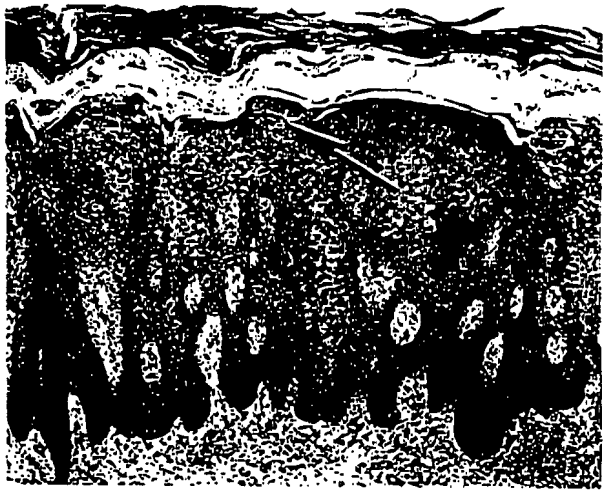

Figure 26–23. Psoriasis. Histologically, established lesions demonstrate marked epidermal hyperplasia, parakeratotic scale, and, importantly, minute microabscesses of neutrophils *(arrow)* within the superficial epidermal layers.

these papillae. This constellation of changes results in abnormal proximity of dermal vessels within the dermal papillae to the overlying parakeratotic scale, and it accounts for the characteristic clinical phenomenon of multiple, minute, bleeding points when the scale is lifted from the plaque **(Auspitz sign)**. Neutrophils form small aggregates within slightly spongiotic foci of the superficial epidermis **(spongiform pustules)** and within the parakeratotic stratum corneum **(Munro's microabscesses)**. In pustular psoriasis, larger abscess-like accumulations of neutrophils are present directly beneath the stratum corneum.

Determination of the pathogenesis of psoriasis is one of the most important challenges in dermatopathologic research. An increased incidence of disease in association with certain HLA types suggests that genetic factors participate in the predisposition for disease development. The genesis of new lesions at sites of trauma (the *Koebner phenomenon*) is undoubtedly providing some basic yet elusive pathogenetic clue. Evidence has recently been accumulated that psoriasis may be a type of complement-mediated reaction localized to the stratum corneum.[54] According to this hypothesis, exogenous or endogenous damage to the stratum corneum of certain individuals results in the unmasking of stratum corneum antigens. These antigens elicit the formation of specific autoantibodies that bind to the stratum corneum, fix complement, and activate the complement cascade. Release locally of C3a, C5a, and C567 then leads to neutrophil activation and accumulation, a phenomenon likely aided by arachidonic acid metabolites, including leukotrienes. Neutrophils within the stratum corneum then release neutral serine proteases, which unmask more antigen and perpetuate the process. Proliferative factors for underlying keratinocytes are released as a consequence of these events and result in increased epidermal turnover and the hyperplasia and scale formation so characteristic of psoriasis.

Another possibility, however, is that the primary defect in psoriasis resides in the enhanced ability of superficial dermal microvessels to recruit neutrophils. It is possible that psoriatic endothelial cells are unusually sensitive to cytokine stimuli that regulate display of endothelial-leukocyte adhesion molecules, possibly as a result of genetically determined enhancement of cytokine receptor expression. Such hypotheses are the subject of active investigation.

LICHEN PLANUS

"Pruritic, purple, polygonal papules" are the presenting signs of this disorder of skin and mucous membranes. Lichen planus is self-limiting and generally resolves spontaneously one to two years after onset, often leaving zones of postinflammatory hyperpigmentation (see later). Oral lesions may persist for years. Malignant degeneration has been noted to occur in chronic mucosal and paramucosal lesions of lichen planus, although the